

1 A Yes.
2 Q They constitute the original preservative system for
3 the Zantac Syrup?
4 A The original antimicrobial preservative system, yes.
5 Q Directing your attention to 71655, production page, the
6 next page, paragraph 5.8.1, can you review that for a moment,
7 Doctor?
8 A Yes, thank you.
9 Q Based on your review and your knowledge, can you
10 confirm that the original formulation for the Zantac Syrup
11 was based on that for the Zantac injection?
12 A Yes, it was.
13 Q Turning to 71656 of plaintiffs' trial exhibit 63, the
14 paragraph that proceeds the heading package, could you
15 review, that, please?
16 (Pause for document examination.)
17 A Yes.
18 Q Based on your review and your knowledge, Doctor, can
19 you confirm that the original Zantac Syrup formulation met
20 the qualifications of the United States Pharmacopeia for
21 microorganisms?
22 A Yes, it was, samplings of the syrup were subjected to
23 the APE tests, abbreviation for antimicrobial preservatives
24 effectiveness test, and the samples were found to comply.
25 Q Directing your attention to page 71676 of plaintiffs'

1 trial exhibit 63, could you review the paragraph 5.8.4
2 entitled Proposed Shelf-Life, Dr. Long?

3 A Yes. We had limited stability data at that time and,
4 therefore, the shelf-life was very conservative, three months
5 at controlled room temperature, and in certain parts of the
6 distribution chain they say it was stored in a refrigerator.

7 Q Now I'm going to ask you to turn your attention to
8 plaintiffs' trial exhibit 244.

9 Doctor, in Exhibit 244, could you turn your

10 attention to page number Y076348 and would you review that?

11 (Pause for document examination.)

12 A Yes, this page describes an amendment to the original
13 IND and it describes how the preservative system was changed
14 after we performed further work and discovered the problem
15 with a particular microorganism, *Pseudomonas cepacia*.

16 Q Is it correct to say, Dr. Long, that although the
17 paraben preservative system of the original Zantac Syrup
18 formulation was sufficient to meet the conditions set forth
19 in the United States Pharmacopeia, another microorganism was
20 subsequently detected?

21 A Yes, it was detected at a later stage after the initial
22 work.

23 Q What is the name of that microorganism?

24 A *Pseudomonas cepacia*.

25 Q Did anything happen as a result of Glaxo's discovery of

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1 the *Pseudomonas cepacia* microorganism problem?

2 A Yes, it brought the project to a screeching halt for a
3 while.

4 Q Can you tell the Court what you mean by screeching
5 halt?

6 A Yeah. At the time we had already submitted a product
7 license application to the regulatory authority in the UK and
8 I was engaged in transferring the process of manufacture of
9 that formulation to our factory in Liverpool and at the same
10 time was directing what we term an in-use test. This is a
11 test where we simulate how the patient would use the product.
12 So that involved taking the top off the bottle, pouring out
13 two five-mil spoons, night and morning, for I think about
14 three weeks, just to see how the product would behave when
15 used by a patient. It's standard practice to make absolutely
16 certain there won't be any surprises when the most important
17 person comes to use that product. And during that exercise
18 we analyzed the contents of the bottle at the end to check
19 that there had been no changes, no significant changes in
20 content.

21 And it was during that period at the end of that
22 test that we had a remarkable finding, and that was that one
23 of the parabens had dramatically decreased in concentration
24 in a period of about three weeks and it was dramatic in that
25 we had other data from sealed bottles where there had been

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1 little change in a period of two years. So something
2 mysterious had happened.

3 Q In addition to the drop in one of the parabens, was the
4 *Pseudomonas cepacia* contamination problem manifested in any
5 other way?

6 A Yes. Yes, we had an intense period of hypothesis as to
7 how could this happen because it didn't fit any known laws of
8 degradation of the parabens, and I sat and I puzzled and I
9 held the bottle, looked at it and thought, and then I was
10 looking inside the cap and I could see a black mark and
11 instinctively I smelled the cap and there was a strong smell
12 of spoilage. Then I thought perhaps we had probably a
13 microorganism here. I immediately contacted our
14 microbiologists and there was an investigation and that's
15 where we found over a million organisms of *Pseudomonas*
16 *cepacia* in each mill of syrup.

17 Q This discovery of the microorganism, the *Pseudomonas*
18 *cepacia* problem that occurred in the first half of 1985; is
19 that correct?

20 A First half, probably June and earlier.

21 Q You were research leader at that point, correct?

22 A Yes.

23 Q And did your responsibilities as research leader
24 include trying to develop an improved antimicrobial
25 preservative system for the Zantac Syrup to overcome this

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1 **Pseudomonas cepacia problem?**

2 A What it did, I had only recently taken on the project
3 and submitted reports to the regulatory submission. I was
4 research leader responsible for the project. I had seen the
5 results of the low preservative content. I had spotted this
6 micro problem by looking at the cap and I felt intimately
7 involved in this problem. It was clearly on my plate.

8 Q Could you turn your attention to plaintiffs' trial
9 exhibit 239, please?

10 (Pause for document examination.)

11 Q Could you identify this document, Dr. Long?

12 A Yes. This is a memorandum faxed across to a colleague
13 based in the States at Glaxo, Inc., informing him of the
14 problem that we had just discovered with the microorganism.
15 The reason I was telling Mr. Chitniss this is that he in
16 parallel was setting up or about to set up stability programs
17 for this inadequately, programs for this inadequately
18 preserved formulation. I immediately wanted to stop him
19 wasting his time. It's another indication of how many
20 parties were involved in this dramatic event which stopped
21 the development.

22 Q So this appearance of this bug brought development work
23 on both sides of the Atlantic to a screeching halt; is that
24 correct?

25 A It did that and it also posed questions about what